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Central Enteric Reference Laboratory & Bureau

1st March, 1953.

Dear Doctor Crézé,

I must apologize for not having written before in response to your letter of the 8th March. I have been away from the laboratory and this explains the delay.

If the observations described in your letter are regularly reproducible they certainly merit to be followed up very carefully. I assume you are not aware of the earlier work on antigenic variation of Salm. typhi and especially of the antecedents of strain H901. I would like to draw your attention to the fact that spontaneous reversion of the Vi-negative variant strain H901 to the Vi-positive form has been observed before.

The history of the strain was given not long ago in the paper in the Journal of Hygiene, 1951, 49, on pages 94-95 and more recently the details were presented in Table 3 of my Discussion Remarks, Oxford Symposium, 1952 [in the Press]. I am sending you under separate cover reprints of these papers, together with those of other papers that may be of interest to you. Kindly return after perusal the 1951 paper that is specially marked, as there are no copies left of this paper.

You will notice from Table 3 in the Discussion Remarks and from page 94 in the 1951 paper that the reverted [rejuvenated] Vi-positive form which Kauffmann (1936) obtained in his mouse experiments with strain H901, was found by Craigie (1938) to belong to Vi-phage Type E1, the same type to which the well-known strain Ty2 belongs, which was isolated during the same outbreak in 1918. I have interpreted this finding as one of the most striking instances of stability of Vi-phage type, which is one of the hereditary traits of the typhoid bacillus.

You wrote in your letter that Nicolle typed your induced mutant strain as belonging to Vi-phage Type A. It is true that Type A may be derived, as a variant, from each of the specific Vi-phage types by the process called "degradation". You will find this described in many of the papers I am sending you, starting from the paper by Craigie and myself (1947). I have marked the relevant pages in some of the reprints. Nevertheless it would be advisable to try to obtain, by the technique you are employing, induced mutants of the strain H901 giving the bacteriophage reactions of Vi-phage Type E1.

I shall send you immediately after the Easter holiday Lemco-stab cultures of the two strains H901 and 0901 and I should be interested to hear whether

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these cultures can be induced to revert to the Vi-positive variant by the procedure you have adopted. Although these Lemco-stab cultures have been prepared only recently they will on plating certainly show a proportion of "rough" variants. At any rate it should not be difficult to obtain typical rough variants starting from these cultures.

If you again obtain variants which you consider to be induced Vi-positive reversions, I shall be glad to examine a number of such cultures for their antigenic composition and Vi-phage type. In this case I would suggest that you select not less than half a dozen cultures, each derived from a single colony. At the same time you could perhaps send also subcultures of the strains mentioned in your letter, that is to say the S and R cultures of H901 from which you started and some of the Vi-positive mutant cultures which had been examined by Dr. Nicolle. Your paratyphoid-B strain Ranson might also be added. The best way of posting the cultures is either in Lemco agar stabs or on small Dorset agar slants.

I hope I have answered your queries to your satisfaction.

Yours sincerely,

(signed) A. Felix

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P.S. Professor Lederberg may have mentioned to you the paper by H.L.Booy and H.L.Wolff on "On the induction of Vi antigen formation in a strain of Salmonella typhi free of Vi antigen", published in "Antonie van Leeuwenhoek", 18, 183, 1952. I would like to draw your attention to the fact that this paper calls for severe criticism. It is evident from the two tables contained in the paper that the authors are not familiar with the method of antigenic analysis. The agglutination tests were carried out by slide agglutination, a technique which has many pitfalls. There were no controls to show the relative sensitivity of the suspensions to O or Vi agglutinins, or to solutions of NaCl, or to normal proteins. Anyone acquainted with the past history of strain H901 will refuse to accept the experiments by Booy and Wolff as evidence of genetic transduction of Vi antigen.

(signed) A.F.